CREOSOTE: EPIDEMIOLOGY AND INCIDENTS

Creosote is a complex chemical mixture of organic compounds. Most compounds in creosote are polyaromatic hydrocarbons (PAHs). An extensive body of literature on creosote and commonly associated substances has been published. The purpose of this chapter is to review the evidence of health effects in humans resulting from exposure to creosote. In particular, the acute and chronic toxicity, teratogenic/reproductive effects, and carcinogenicity are discussed. Two approaches are used in this section:

- The potential acute health effects of creosote in humans, reported as incident reports from different sources, are summarized.

- A literature search of chronic health effects associated with creosote exposure, including results of epidemiological studies, are summarized.

4.1 INCIDENT REPORT DATA ASSOCIATED WITH HEALTH EFFECTS OF CREOSOTE EXPOSURE

There are many incident reports of health effects associated with acute creosote exposure. The following databases have been consulted for the poisoning incident data on the active ingredient creosote (PC Code: 025002):

1. **OPP Incident Data System (IDS)** - The Incident Data System of The Office of Pesticide Programs (OPP) of the Environmental Protection Agency (EPA) contains reports of incidents from various sources, including registrants, other federal and state health and environmental agencies and individual consumers, submitted to OPP since 1992. Reports submitted to the Incident Data System represent anecdotal reports or allegations only, unless otherwise stated. Typically no conclusions can be drawn implicating the pesticide as a cause of any of the reported health effects. Nevertheless, sometimes with enough cases and/or enough documentation risk mitigation measures may be suggested.

2. **Poison Control Centers** - as the result of a data purchase by EPA, OPP received Poison Control Center data covering the years 1993 through 1996 for all pesticides. Most of the national Poison Control Centers (PCCs) participate in a national data collection system, the Toxic Exposure Surveillance System, which obtains data from about 65-70 centers at hospitals and universities. PCCs provide telephone consultation for individuals and health care providers on suspected poisonings, involving drugs, household products, pesticides, etc.

3. **California Department of Pesticide Regulation** - California has collected uniform data on suspected pesticide poisonings since 1982. Physicians are required, by statute, to report to their local health officer all occurrences of illness suspected of being related to exposure to pesticides. The majority of the incidents involve workers. Information on exposure (worker activity), type of illness (systemic, eye, skin, eye/skin and respiratory), likelihood of a causal relationship, and number of days off work and in the hospital are provided.

4. **National Pesticide Telecommunications Network (NPTN)** - NPTN is a toll-free information service supported by OPP. A ranking of the top 200 active ingredients for which telephone calls were received during calendar years 1984-1991, inclusive, has been prepared. The total number of calls was tabulated for the categories human incidents, animal incidents, calls for information, and others.

5. **Published Incident Reports** - Some incident reports associated with creosote related human health hazard are published in the scientific literature.

4.1.1 OPP's Incident Data System (IDS)

Please note that the following cases from the IDS do not have documentation confirming exposure or health effects. Registrants are not required to report incidents involving exposure to previously treated wood, only direct exposure to creosote itself. Therefore, it is possible that serious adverse effects involving exposures to treated wood have been missed by this review. Legal claims of severe damage to eyes and skin including infections requiring amputation have been reported but only in a cursory way and without enough documentation to be included in this review.

Incident#2796-100

An incident was investigated in the United Kingdom in 1994 or 1995 (date of incident unknown) involving creosote. After a landlord treated a residence with creosote the male tenant complained of headache, stomach ache, and respiratory irritation. No further information is available on the disposition of this case.

Incident #2796-119

An incident was investigated in the United Kingdom in 1994. After creosoting work was done on the flat below theirs, a male and female reported tearing, burning throat, nausea, and vomiting. No further information is available on the disposition of this case.

Incident #8760-1

In 1997 a 38 year old railroad worker alleged inhalation and dermal exposure to creosote. The timing and duration of exposure are not reported. A legal claim has been filed alleging nodular malignant melanoma. No further information is available on the disposition of this case.

Incident #8760-3

A worker at a creosote plant was exposed in 1994 while testing boring treated wood. He reportedly developed skin rash on wrists and forearms and visited a dermatologist.

4.1.2 Poison Control Center

No data were reported in the Poison Control Center database covering the years 1993 through 1996**.**

4.1.3 California Data - 1982 through 1996

Detailed descriptions of 124 cases submitted to the California Pesticide Illness Surveillance Program (1982-1996) were reviewed. In 114 of these cases, creosote was used alone and was judged to be responsible for the health effects. Only cases with a definite, probable or possible relationship were reviewed. Creosote ranked 88th as a cause of systemic poisoning in California (1982-1994). **Table 4-1** presents the number of cases due to creosote exposure reported by year. **Table 4-2** gives the total number of workers that took time off work as a result of their illness and how many were hospitalized and for how long.

Table 4-1:
Cases Due to Creosote Exposure in California Reported by Type of Illness and Year, 1982-1996

Year	Number of Cases			
	Handling Creosote	Exposed to Treated Wood	Unknown	Total
1982	10	4	5	19
1983	3	3	-	6
1984	14	3	-	17
1985	15	2	2	19
1986	3	1	-	4
1987	5	5	-	10
1988	3	5	-	8
1989	5	2	1	8
1990	2	3	1	6
1991	-	6	-	6
1992	1	4	-	5
1993	-	2	-	2
1994	1	-	-	1
1995	-	2	-	2
1996	-	1	-	1
Total	62	43	9	114

Table 4-2:
Number of Persons Disabled (taking time off work) or Hospitalized for Indicated Number of Days After Creosote Exposure in California, 1982-1996.

	Number of Persons Disabled	Number of Persons Hospitalized
One day	9	-
Two days	12	1
3-5 days	7	-
6-10 days	2	-
more than 10 days	-	-
Unknown	6	-

Most of the cases that could definitely be attributed to creosote (80% of the 50 cases categorized as definite) involved workers who handled creosote directly but did not have proper protection for eyes or skin. A significant number of cases have resulted when workers have been exposed to treated wood, usually by handling or sawing the wood. Most of these cases experienced chemical burns to the skin or eyes. The number of cases due to handling creosote versus the number due to handling treated wood are presented in **Table 4-3** below.

Table 4-3:
Illnesses by Activity Categories for Creosote Exposure in California, 1982-1996

Activity Category	Number of Cases			
	Handling Creosote	Exposed to Treated Wood	Unknown	Total
Applicator	62	43	9	114

4.1.4 National Pesticide Telecommunications Network (NPTN)

On the list of the top 200 chemicals for which NPTN received calls from 1984-1991 inclusively, creosote was ranked 118th with 26 incidents in humans reported and no incidents in animals.

4.1.5 Incident Reports Associated with Acute Toxic Effects of Creosote Published in Scientific Literature.

Dean et al. (1992) reported on a white ten week old female, who weighed 6 kilograms, and experienced cyanosis, irritability, metabolic acidosis, and a lethal methehemoglobin level of 71.4%. She was taken to the hospital and remained for three days. Three days earlier, the child's father replaced an aluminum stove pipe leading from the wood-burning stove to the chimney and installed a straight section of the stove pipe. Green slab pine wood was continuously burning in the stove. Pine tar fumes emitted from the stove were the suspected source of creosote oils. The girl's cradle was approximately five feet from the stove.

Bowman et al. (1984) reported on a seventy year old man who was found unconscious with a cup of creosote beside him. On admission to the hospital, the man's respiratory effort was weak and on auscultation, widespread crackles were heard. His face and clothes were stained with vomit and creosote. He was immediately administered endotracheal intubation and artificial ventilation. He experienced anuria and died. After his death, a liter of mostly creosote fluid was found in his stomach.

Thompson et al. (1994) reported that during 1989 to 1991, 250 children (124 boys and 126 girls) under 10 years old out of 6, 478 cases were taken to accident and emergency departments in the United Kingdom for suspected pesticide poisoning. Seven percent of these cases were due to creosote.

The following excerpts were taken directly for the Hazardous Substances Data Bank (HSDB). HSDB is a toxicology data file on the National Library of Medicine’s Toxicology Data Network (TOXNET). Data are derived from "a core set of books, government documents, technical reports and selected primary journal literature. HSDB is peer-reviewed by the Scientific Review Panel (SRP), a committee of experts in the major subject areas within the bank’s scope."

> Death from large doses of creosote appears to be due largely to cardiovascular collapse. Fatalities have occurred 14 to 36 hr after the ingestion of about 7 g by adults or 1 to 2 g by children. The symptoms of systemic illness included salivation, vomiting, respiratory difficulties, thready pulse, vertigo, headache, loss of pupillary reflexes, hypothermia, cyanosis, and mild convulsions. The repeated absorption of therapeutic doses from the gastroenteric tract may induce signs of chronic intoxication, characterized by disturbances of vision and digestion (incr peristalsis & excretion of bloody feces). In isolated cases of "self-medication," hypertension & also general cardiovascular collapse have been described.
> *[Clayton, G. D. and F. E. Clayton (eds.). Patty's Industrial Hygiene and Toxicology: Volume 2A, 2B, 2C: Toxicology. 3rd ed. New York: John Wiley Sons, 1981-1982. 2603]*

Contact of creosote with the skin or condensation of vapors of creosote on the skin or mucous membranes may induce an intense burning and itching with local erythema, grayish yellow to bronze pigmentation, papular & vesicular eruptions, and gangrene and in isolated instances cancer. ... Heinz bodies have been noted in the blood of a patient one yr after his exposure to creosote. ... Similar observations following percutaneous absorption of this preparation. Eye injuries can include keratitis, conjunctivitis, and abrasion of the cornea. ... Permanent corneal scars result in about one third of such cases. Photosensitization has been reported ... and severe systemic illness.
[Clayton, G. D. and F. E. Clayton (eds.). Patty's Industrial Hygiene and Toxicology: Volume 2A, 2B, 2C: Toxicology. 3rd ed. New York: John Wiley Sons, 1981-1982. 2603]

Contact of liquid creosote with the eye has caused painful protracted keratoconjunctivitis. This has involved loss of corneal epithelium, clouding of the cornea, miosis, and long lasting irritability and photophobia. In one report concerned with creosote, two patients have been described, one examined 2 wk and the other 2 months after working with this material, both complaining of haziness of vision, which was found to be associated with numerous gray spots of varied size in the corneas, plus a superficial keratitis.
[Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986. 283]

Injuries to the skin or eyes have occurred mainly among men engaged in dipping or in "pickling" and handling "sleepers," mine timbers, and woods for floors and other purposes. ... Calls attention to burns induced by fine particles of sawdust from creosote-treated lumber. ... The burns were reduced to a minimum on rainy days, probably because of the decreased dispersion of both the wood particles and creosote.
[Clayton, G. D. and F. E. Clayton (eds.). Patty's Industrial Hygiene and Toxicology: Volume 2A, 2B, 2C: Toxicology. 3rd ed. New York: John Wiley Sons, 1981-1982. 2601]

Epitheliomas can result from prolonged exposure to creosote.
[Kirk-Othmer Encyclopedia of Chemical Technology. 3rd ed., Volumes 1-26. New York, NY: John Wiley and Sons, 1978-1984.,p. V22 592 (1983)]

Vapor causes moderate irritation of nose and throat. Liquid may cause ... reddening and itching of skin.
[U.S. Coast Guard, Department of Transportation. CHRIS - Hazardous Chemical Data. Volume II. Washington, D.C.: U.S. Government Printing Office, 1984-5.]

Old creosote treated lumber ... retains a considerable portion of the oil for periods up to 25 or 30 years.
[Clayton, G. D. and F. E. Clayton (eds.). Patty's Industrial Hygiene and Toxicology: Volume 2A, 2B, 2C: Toxicology. 3rd ed. New York: John Wiley Sons, 1981-1982. 2604]

4.2 EPIDEMIOLOGIC STUDIES ASSOCIATED WITH HEALTH EFFECTS OF CREOSOTE IN HUMANS

To summarize the epidemiologic studies associated with creosote exposure, considerable attention was given to presenting the information collected during the review in as logical a format as possible. Reviewed papers are primarily organized according to the type of epidemiologic method followed, i.e., case series involving chronic effects, cross-sectional, case-control, and cohort studies.

1. Case Series Involving Chronic Effects

In addition to the acute incidence report summarized in **Section 4.1**, some chronic health effects are also reported after exposure to creosote and related compounds. Because of the long latency period after exposure, the cause-effect relationship may not be apparent. These reports also are summarized in this document.

2. Cross-sectional Study

This kind of study usually is done by conducting a survey on a group of people or a community, perhaps stratified by age, sex, ethnicity, working environment etc., but at one point in time or over a short time interval. Although a snapshot, horizontal surveys of prevalence and intensity within different age classes of a community can nevertheless provide valuable information on the rate at which individuals acquire exposure to a source of risk through time, provided that the exposed population and the source of the risks have remained approximately stable for a period of time. With statistical approaches, potential association of the risk factors (exposure) and disease is suggested.

3. Cohort Study

Cohorts studies evaluate individuals selected on the basis of their exposure to the agent under study and monitored for development of disease. Prospective studies monitor individuals who initially are disease-free to determine if they develop the disease over time.

4. Case-Control Study

In case-control studies, subjects are selected on the basis of disease status: disease cases and matched-cases of disease-free individuals. The exposure histories of the two groups are compared to determine key consistent features.

Within each category of epidemiologic study, the information in this document includes (1) population investigated, (2) what health effects and other effects were found, and (3) what level of confidence should be assigned to the study results. **Table 4-4**, attached at the end of this section, summarizes the results of the studies reviewed for this document.

4.2.1 Case Series Involving Chronic Effects Associated with Health Effects of Creosote in Humans

4.2.1.1 Garrett (1975)

In a letter-to-the-editor, Garrett reported two patients diagnosed within eighteen months with multi-focal transitional cell carcinoma of the bladder with muscle invasion. Both men were determined to have had chronic exposure to cresol and creosote, but no details of the exposures were provided.

Reports of this kind may be useful when combined with other reports and studies. Considered alone, no conclusion regarding association of exposure to creosote with development of bladder cancer can be made.

4.2.2 Cross-Sectional Studies Associated with Health Effects of Creosote in Humans

4.2.2.1 Koppers (1979a)

The Koppers Company sponsored a cross-sectional study of workers at four wood preservative plants in Pennsylvania, South Carolina, West Virginia, and Kentucky where creosote and creosote/coal tar were the predominant treatments. The study was specifically aimed at identifying any health problems known to be related to exposure to these major process materials. An array of medical examinations were performed on 257 participants (73% of 351 total workers). The ratios of men to women participants were similar among all four plants. However, the ratios of black to white workers differed significantly among the plants, therefore the ratios of black to white participants differed also. The battery of examinations included a medical questionnaire, chemical exposure questionnaire, chest x-ray, pulmonary function test, clinical chemistry analysis, hematology analysis, urinalysis, sputum cytology exam, and urine cytology exam.

No exposure parameter was evaluated in the health assessment other than length of service. With the exception of a greater than expected number of pustular eruptions of the skin, all other tests revealed only infrequent and borderline abnormal findings. There was no evidence of cancer at any site associated with work at these plants.

Due to the broad nature and limited depth of this study, only gross negative health effects could be observed. Since no exposure assessment for creosote was performed, no association between observed health conditions and creosote exposure was possible. Within these limitations, no evidence of detrimental health effects from working with creosote was seen.

4.2.2.2 Koppers (1979b,c and 1980a,b,c)

Cross-sectional studies were conducted at five coal tar processing plants to assess the health status of the work forces and thereby identify possible adverse health problems associated with exposure to coal tar and its derivatives. The studies were conducted by contracted researchers as part of a continuing health and safety program sponsored by the parent organization. The five plants studied were located in California, West Virginia, Alabama, Ohio, and Illinois; all five provided potential exposure to many industrial products, including creosote, resulting from distillation of coal tar. From a toxicological evaluation of coal tar products, an appropriate medical examination protocol was designed to measure a number of health parameters that should reveal toxic effects from the target coal tar products. Included among the procedures were collection of medical and work history, chest x-ray, pulmonary function test, clinical chemistry analysis, blood and urological analysis, and sputum cytology examination.

The study populations included men and women, white and black, but participation was voluntary resulting in an overall participation rate of 42%. Length of employment ranged between less than one year to 50 years, but a majority of the workers who participated in the study worked 10 years or less. No assessment of personal exposure to specific substances was performed. The sole exposure parameter, which was collected through the work history questionnaire, was the number of years of potential exposure to coal tar and its derivatives.

Among the results from the broad medical examination, a number of excesses and atypical findings were observed, although few could be directly associated with working at the coal tar plants. Restrictive respiratory deficits were found in the populations at all of the study sites and considerable excesses were seen at three sites. A few individuals at four of the five plants also were observed with obstructive respiratory deficits. Increases in gamma glutamyl transpeptidase (GGTP) and lactic dehydrogenase (LDH) levels were found in a few individuals at two plants. Results from hematological examinations showed atypical cells or abnormal cell counts in a few workers at all five plants. Of particular interest were the increased eosinophil counts observed in 13% of the workers at one plant. The only notable result from the urine analyses was the observation of excess RBCs (eight workers) and WBCs (11 workers) in 10% of the participants from one plant. The prevalence of folliculitis was greater than expected at three of the plants, with one of the plants having an incidence significantly increased (11 out of 105 workers examined). At one plant, no folliculitis was seen, but tar warts which are known to be associated with exposure to coal tar, were in excess. In general, few atypical cells were found during examinations of sputum. One exception was the increased C-reactive protein observed in five workers at the same plant at which the excess blood cells in urine and the greatest excess in folliculitis occurred. No cancer at any site was discovered during the broad medical examination program.

This group of studies showed evidence of increased prevalence of folliculitis and tar warts consistent with prolonged exposure to coal tar products. The only chronic health effect observed was an excess of restrictive respiratory deficit. No excess cancer occurrence was reported. The usefulness of results of this study are weakened by the lack of specificity to creosote exposure, by

only 42% participation of eligible workers, and the lack of individual exposure assessment to coal tar products.

4.2.2.3 NIOSH (1981)

Following a request from a carpenters' union, NIOSH conducted an evaluation of exposure among six dock builders engaged in driving creosote-preserved logs into a river bottom. Health surveys also were administered for five of the six dock builders.

Breathing zone and area air concentration measurements collected for the cyclohexane-extractable fraction of the coal tar pitch volatiles ranged from below the detectable limit to 0.06 mg/m^3. However, because of atypical weather conditions on the day of sampling and because the pile driver was in operation for less than one hour, the industrial hygiene results were not representative of normal working conditions.

A medical questionnaire was administered to five of the six workers. The questionnaire covered work conditions and work history, past exposures, current health problems, medical history, the use of personal protection and personal hygiene. Questions on health problems focused on skin, respiratory, gastrointestinal, and central nervous system problems. The five participating workers were also given skin examinations. The pile drivers were between 24 and 61 years of age (average age 44.6 years), and all had worked at the current site for at least five months. All of the participants had been employed as pile drivers for an average of 16.6 years of which an average of 8.3 years had involved pile-driving creosote-preserved piles. A number of health problems were reported by the workers, including eye irritation, nausea, lightheadedness, and swelling of the face, eyes, and hands. Skin problems reported by the workers included irritation, rashes, erythema, burning, dryness, desquamation, itching, and cracking. On hot days, symptoms were reported to be worse, and in addition, the workers experienced tearing and burning eyes, red eyes, swollen or puffy eyes, and photophobia. Four of the five workers responding to the questionnaire reported that their visual acuity had gradually worsened.

Skin examinations of the workers revealed erythema on the face, neck and hands, dry skin with desquamation in sun exposed areas, black comedones, plugged hair follicles on hands and forearms, and mild folliculitis on the forearms.

The symptoms reported by the dock building workers and the observations made during skin examinations were consistent with phototoxic skin reactions. The folliculitis was consistent with prolonged and direct contact with creosote. No chronic health effects, including cancers, were reported or observed, and because of the small number of workers examined, encountering these diseases would not be expected.

4.2.2.4 EPA (1981a)

A broad health evaluation was performed in 1981 on 59 workers (total of 79 workers eligible) at a wood preservative treatment plant in Ohio. The workers (51 males, eight females) were aged between 20 and 69 years, with only a slightly higher frequency of workers aged between 55 and 59 years. Creosote had been used at the plant since the 1920s, but had been discontinued in 1979. A large battery of tests including chest x-rays, pulmonary function tests, clinical chemistry analyses, hematology and urology analyses, and sputum and urine cytology were used to assess effects on organs and body systems known to be at risk from exposure to chemicals used in the plant. No industrial hygiene monitoring data were available, and no exposure assessments for individual participants were made.

Fifteen workers were observed with restrictive or obstructive respiratory deficits. One participant had elevated serum enzyme levels indicative of liver disease. Two workers had proteinuria and one other had evidence of urinary tract inflammation. Thirteen workers were found to have elevated serum triglycerides, but only one with levels above 400mg/100ml.

This study identified no occupationally related disease and showed little evidence of chronic effects from working for long periods in a wood preservative treatment plant. The small size of the study cohort and the lack of assessment of individual exposures, including the absence of data on number of years employed, seriously limited the possibility of observing negative health effects.

4.2.2.5 EPA (1986)

A cross-sectional study was conducted on 113 of the total 140 workers at a lumber preservative treatment plant. Thirty-nine of the participants worked less than one year, 40 had worked between one and 10 years, and 34 had worked between 11 and 35 years. The plant had used creosote, creosote/tar solution, Wolman salt (CCA), and pentachlorophenol (PCP) for many years since 1946 as wood preservatives. A fire retardant, NCX, also was used since 1978. The study focused on creosote and PCP since these were considered the chemicals of concern.

Health effects from working at the wood treatment plant were evaluated by a battery of tests including chest x-ray, pulmonary function test, clinical chemistry analysis, hematology and urology analyses, and sputum and urine cytology studies. Detailed medical and work history questionnaires were administered, however, no individual exposure assessment was conducted. Air concentrations for coal-tar pitch volatiles were available from a single industrial hygiene survey conducted in 1978.

No evidence of skin cancer, bladder cancer, or lung cancer were seen in the study population. Pustular eruptions likely related to exposures at the plant were observed in a greater than expected number of workers. A number of workers had restrictive or obstructive pulmonary deficits, and two workers showed evidence of liver disease. There was no evidence of kidney disease or blood disease.

This study showed little evidence of chronic effects from working for long periods in a wood preservative treatment plant. The small size of the study cohort and the lack of assessment of individual exposures limited the possibility of observing negative health effects.

4.2.3 Cohort Studies Associated with Health Effects of Creosote in Humans

4.2.3.1 EPA, (1981b and 1982)

An in-depth study of mortality in 4048 males who worked at eight Koppers coal tar plants was conducted by Tabershaw Occupational Medicine Associates and reported by Koppers in 1981. The plants were located in Illinois, West Virginia, California, New Jersey (two plants), Texas, Alabama, and Ohio; and all plants except for one of the New Jersey plants distilled crude coal tar. Creosote was among the distillation by-products resulting from the plants' operations . The cohort was initially defined as all males who worked at least 10 days between 1946 and 1977. Persons who worked in strictly clerical or secretarial positions were excluded, as were women because of their small number.

The cohort consisted of 2,150 workers (53.1%) known to be white, 1,104 workers (27.3%) known to be black, and 794 workers (19.6%) whose race was unknown. Demographic information including date of hire, date of termination, and complete work history was collected from plant personnel files. Vital status follow-up information was collected by using plant records, SSA, motor vehicle bureaus, and finally local phone directories. The total cohort provided 64,600 person-years of observation with 9,917 person-years attributed to workers whose race was unknown. Of the total cohort, 703 (17.4%) were identified as deceased, and the vital status of 359 (8.9%) remained unknown.

During the analysis of the 1981 study, it was recognized that the lack of race information for almost 20% of the cohort presented a serious weakness in the study and imposed considerable difficulties with the interpretation and validity of results. This was further complicated by the fact that 163 of the workers classified as "race unknown" also had unknown vital status. Because of this weakness, a re-analysis of data for only those workers whose race was verified was performed in 1982, therefore, the results from the 1981 study are not presented here. The redefined cohort excluded the 794 workers with unknown race. The number of person-years of follow-up was 36,635 for the white workers and 18,047 for the black workers. Within the cohort, 701 deaths had occurred by the close of the study (12/31/77), and death certificates were retrieved for 632 workers (359 white, 273 black).

The second analysis looked at cause-specific deaths for six subgroups of the total population of workers with known race. These groups were (1) all white workers, (2) white workers employed for less than six months, (2) white workers employed for six months or more, (4) all black workers, (5) black workers employed for less than six months, (6) black workers employed for six months or more.

For the entire population of white workers, the standard mortality ratio (SMR) for all causes was 109. However, the SMR for deaths from all cancers was considerably elevated (SMR=126) largely due to the significant excess in cancers of the lung (SMR=160, p=0.05). Excesses also were observed for cancers of the stomach, large intestine, rectum, bladder, and kidney, however, none of the SMRs were statistically significant. When only white workers employed for less than six months were considered, a large excess in total mortality was observed (SMR=137, p=0.01), and the SMR for deaths from all cancers was 125, though not significant. The increases in overall mortality were due largely to significant excesses in deaths from cirrhosis of the liver (SMR=340, p=0.01), accidents (SMR=238, p=0.01), and cancer of the stomach (four observed, 0.74 expected, SMR=540, p=0.05). When only white workers employed for six months or more were considered, the only significant excesses observed were for cancer of the respiratory system (SMR=182, p=0.01), largely due to an excess of lung cancer (SMR=180, p=0.01). Deaths from all other cause-specific cancers were within expected numbers.

For the combined population of black workers, a number of statistically significant excesses (p=0.05) were found, including deaths from all causes (SMR=113), all cancers (SMR=138), cancer of the rectum (SMR=439), and lung cancer (SMR=173). The number of deaths from accidents, poisoning, and violence were also highly elevated (SMR=186, p=0.01). When only black workers employed for less than six months were considered, large excesses were seen for total mortality (SMR=154, p=0.01), for deaths from all cancers (SMR=171, p=0.05), and for accidents (SMR=241, p=0.01). The SMR for cancer of the respiratory system was significantly increased (226, p=0.05), influenced greatly by the SMR for lung cancer (SMR=243, p=0.01). The SMR for cancer of the esophagus was also greatly increased (326), though it was based on only three deaths with 0.92 expected. When only black workers employed for more than six months or more were considered, the SMR for all causes of death was 90, and the only significant excess observed was for bladder cancer (SMR=531, p=0.05) based on three deaths. Nonsignificant excesses also were observed for deaths from all cancers and several specific diseases, including cancers of the digestive system and skin, diseases of the hematopoietic system, and accidents. None of the excesses were statistically significant and were based on small numbers of deaths. Overall, mortality in the group of black workers employed six months were higher than in the black workers employed less than six months.

This study provided a large amount of mortality data on a reasonably large occupational cohort. Moderately convincing evidence is presented that employment at the eight coal tar distillation plants may result in increased risk of death from a range of malignancies. The study appeared to be well planned and executed, though the validity of the findings is limited by a number of shortcomings. These include the lack of race information on a large fraction of the cohort, the small number of deaths observed for many of the diseases reported in excess, and the very crude measure of exposure based only on employment at one or more of the plants.

4.2.3.2 Steineck et al. (1989)

Steineck, et al. employed a complex job-exposure matrix to estimate exposure for calculating relative risk for development of renal pelvic cancer (RPC) or bladder cancer (BC) in a Swedish population. The cohort was defined as all males born in Sweden, aged 20-64 in 1960, who reported themselves employed. Cases of renal RPC or BC occurring during the 19-year study period were identified through the National Swedish Cancer Registry.

The job-exposure matrix used to determine exposed and unexposed subpopulations was based on self-reported job-related information collected in 1960 for census purposes. Based on this information, subjects were classified into 292 occupational titles and 308 industrial categories, yielding 292 X 308 possible work tasks. Potential exposure to 50 single agents or groups of substances were assigned for each possible work task defined by the matrix. Among the potential exposures selected for evaluation were most of those cited in the literature as potential risk factors for the two cancers of interest, and creosote.

Relative risks were calculated after adjusting for age in 1960 (six categories). For some calculations, adjustments also were made for marital status, socioeconomic group, and urbanization of residence. Among the total study population of 1,905,660 persons, 556, 429 were judged to be exposed to at least one of the selected substances. During the 19 years of observations within the study, there were 714 cases of RPC with 542 cases occurring among the unexposed subjects. There were 10,123 cases of BC with 7,432 cases occurring within the unexposed group. For individuals categorized as exposed to creosote, the relative risk for BC was 1.4 (95% CI 0.7-2.6) compared to cohort members not assigned any exposure. It is notable that all of the BC cases categorized as exposed were leather tanners who were also assigned a number of other exposures. When adjustments for applied for age, marital status, socioeconomic group, and degree of urbanization, the relative risk for BC remained between 1.25 and 1.30.

This study provides very limited evidence of association between exposure to creosote and occurrence of bladder cancer. Weaknesses include exposure assessment based solely on self-reported occupational information from a single census observation, lack of control for multiple exposures, and no consideration for nonoccupational exposures.

4.2.3.3 Karlehagen et al. (1992)

Karlehagen, et al. studied cancer incidence among 922 men exposed to creosote at 13 wood impregnating plants in Sweden and Norway. Most participants worked as impregnators while 36 men repaired or maintained railroad cars used to transport creosote. Study participants were employed at least one year between 1950 and 1975, and follow-up was 1958-1985 for the workers in Sweden and 1953-1987 for the workers in Norway. Cancers were identified through national cancer registries in both countries. Cancer registration is compulsory in both countries, and quality and completeness of the registries was considered to be good.

No individual exposure measurements were available for participants, however, levels of naphthalene and benzo(a)pyrene (major constituents of creosote) at several of the plants had been determined to be 0.1-11 mg/m^3 and 0.03$\mu g/m^3$, respectively. Levels for both constituents were well below accepted exposure limits. Consequently, exposure assessment for study participants was based on minimum length of employment at plants known to use creosote regularly. Information on the type of work performed at each plant was collected through use of a questionnaire completed by plant personnel, but not by participants. No differences in exposure conditions among the 13 plants were observed.

The total incidence of cancer was lower than expected with 129 cases observed and 137 cases expected. Some differences were seen between the Swedish and Norway subgroups but the differences were small. Increased risks were observed for lip cancer (SIR=2.50, P=0.05), nonmelanoma skin cancer (SIR=2.37, P=0.02), and malignant lymphoma (SIR=1.9, P=0.06). When a latency period of 20 years since first exposure was applied, the SIRs for lip cancer, nonmelanoma skin cancer, and malignant melanoma were 3.7, 2.0, and 2.2 respectively. Only the SIR for lip cancer (five cases observed, 1.34 cases expected) was statistically significant. No increase in the incidence of lung cancer was observed in this population, with or without consideration for time since first exposure.

This study presents reasonable evidence that exposure to creosote, as measured by employment at creosote plants, is likely associated with development of nonmelanoma skin cancer. Increased risks of lip cancer and malignant melanoma (Norway subgroup only), and malignant lymphoma were also observed in the study population, but the risks were not statistically significant. Because the workers in the study worked outdoors part of the time, the validity of the associations observed, particularly for lip cancer, nonmelanoma skin cancer, and malignant melanoma, may be weakened.

4.2.4 Case Control Studies Associated with Health Effects of Creosote in Humans

4.2.4.1 Flodin et al. (1987)

Risk factors for development of multiple myeloma (MM) were investigated in a study of 131 cases and 431 controls in Sweden. The cases were identified from records at six hospitals in southeast Sweden and were required to be less than 81 years of age, of Swedish ethnicity, resident in the catchment areas of the hospitals at the time of diagnosis, and capable of responding to a questionnaire. The 131 cases represented approximately one third of the total number of MM cases occurring in the area as reported to the cancer registry. The discrepancy between total number of cases and the number of cases identified from the six hospitals was attributed to simple administrative record keeping and was judged to not impose any bias on the study findings. Controls were randomly selected from population registries for the same catchment areas from which the cases were drawn. Differences in average age and distributions of gender were found between cases and controls. The average age for cases was 64 years and for controls, 58 years. Within the 131 cases, 57 percent were males; within 431 controls, 46 percent were males.

Assessment of exposure was through a nine-page questionnaire consisting of 17 major questions of which 10 related to occupational exposures. Some of the occupational questions also asked further questions regarding details of exposures. Reported exposures lasting less than one year and all reported exposures within five years prior to diagnosis were ignored in the analyses.

Crude rate ratios were significantly increased for occupational exposure to creosote (RR=6.0, 95% CI 2.00-18.2), fresh wood, engine exhaust, farming, and bricklaying. When the cases and controls were stratified into four age groups, the elevated risk ratios remained for creosote, fresh wood, and engine exhaust. The increased risks associated with creosote, engine exhaust, and fresh wood also remained significant when analyses controlled for confounding effects of other determinants.

This study provides moderate evidence that exposure to creosote, as measured by self-reporting via mailed questionnaire, may be linked to development of MM. The association is less convincing because the numbers of cases and controls reporting exposure to creosote were quite small. Also, the study suffers the same limits as other studies using similar assessment methods.

4.2.4.2 Persson et al. (1989)

A case-control study was conducted in Sweden by Persson, et al. to investigate associations between exposure to creosote and subsequent development of Hodgkin disease (HD) or non-Hodgkin's lymphoma (NHL). Cases were 160 patients (101 men, 59 women) with HD or NHL identified through the registry at Orebro Medical Centre Hospital and diagnosed between 1964 and 1986. The cases remained alive at least through the data collection period in 1986 and were required to be at least 20 years of age at diagnosis, born in Sweden, living in the area of the hospital at time of diagnosis, less than 80 years of age at time of data collection, and mentally capable of responding to the study questionnaire. The 275 controls (157 men, 118 women) were a subset of a larger set of controls, previously used in earlier studies, randomly drawn from general population registries in catchment areas of several hospitals. For the current study, only individuals in the catchment area from which the patients were drawn were used as controls. The controls were required to meet the applicable inclusion criteria used for patients.

Information for assessment of exposures was collected through a nine page questionnaire mailed to each case and control. Of 17 main questions, 10 questions addressed occupational exposures with some of the occupational questions having additional subquestions asking for details. Questions also were asked about exposures during leisure activities. Exposures reported for periods of less than one year were not considered. A latency period between exposure and development of disease was imposed by considering only exposures within five to 45 years prior to diagnosis for the cases. For the controls, exposures were only considered if they occurred five to 45 years before the point in time of selection.

Age ranges for cases and controls were similar; 20-73 for HD, 22-79 for NHL, and 20-77 for controls. Crude odds ratios (ORs) for both HD and NHL were increased for exposure to wood

preservatives and for exposure to creosote specifically (OR 10.5 for HD, OR 13.6 for NHL). Although the numbers of cases and controls exposed to creosote were small, logistic analyses were performed to control for age at time of case diagnosis, gender, and two exposure determinants, i.e., farming and exposure to fresh wood. For HD, the logistic OR for occupational exposure to creosote was still elevated (OR 10.7, CI 90% 1.1-103). For NHL, the logistic OR was 9.4 (CI 90% 1.2-69).

Assuming the instrument for exposure assessment and the methodology for administration was not biased, this study provides good evidence that exposure to creosote is a risk factor for development of both HD and HNL. The study is somewhat weakened by the small of number of persons reporting creosote exposure.

4.2.4.3 Feingold et al. (1992)

Feingold, et al. studied associations between parental exposures and cancers in children born subsequent to the exposures. The 252 incident cases, identified from a Colorado cancer registry, were in children 0-14 years of age, diagnosed between 1976 and1983. The cases were compared with 222 controls selected by random digit dialing in the same geographical area as the cases and matched on age (+/- three years), gender, and telephone exchange area.

Assessment of parental exposure was based on job history information (including job title, industry, and employment dates) collected by personal interview. A job-exposure matrix, derived from past industrial hygiene surveys and knowledge of industrial processes, was used to assign exposures to individuals on the basis of job title and industry of employment. All jobs held for six months or longer by mothers and fathers during the year prior to birth of the child were linked to all chemicals assigned to the job. Analyses were then performed to determine associations between cancer incidence and parental exposure to a large number of substances.

Creosote was not identified as an exposure for any of the mothers of cases or controls. An adjusted odds ratio of 2.5 (CI = 0.8-8.1) was found for association of fathers' exposure to creosote during the year prior to birth of children with any type of cancer in the offspring. When associations between fathers' exposure to creosote and the incidence of specific cancers in children born subsequently were investigated, an odds ratio of 3.7 (CI = 0.8-16.6) was observed for childhood brain cancer. Fathers assigned exposure to creosote were chiefly in the construction industry or were farmers.

The major limitation of this study is the imprecision of the exposure assessment. Exposures to individuals with the same job titles and working in the same industries vary widely. Therefore, assignments of exposures to specific chemicals, such as creosote, based entirely on job titles and industries may be invalid for some individuals. Also, the credibility of occupation information collected from mothers for fathers is likely to be only 60-80%. However, exposure misclassification resulting from the lack of individual exposure data, or due to the necessary use of information from surrogates, is likely to be equal among parents of cases and controls and therefore, should be nondifferential.

4.2.4.4 Persson et al. (1993)

A case-control study was conducted in Sweden by Persson, et al. among 124 patients with HD or NHL to reexamine earlier findings of associations between exposure to creosote and HD and NHL. Cases diagnosed between 1975 and 1984 were identified through a regional cancer registry located at a university hospital serving a three county area. Only men were included in the study, and were required to be at least 20 year of age, born in Sweden, living in the area of the hospital at time of diagnosis, less than 80 years of age at time of data collection and mentally capable of responding to the study questionnaire. The 204 controls were randomly drawn from general population registries for the catchment area of the university hospital from which the patients were drawn. The controls were required to meet the applicable inclusion criteria used for patients.

Information for assessment of exposures was collected through a nine page questionnaire mailed to each case and control. Of 17 main questions, 10 addressed occupational exposures with some of the occupational questions having additional subquestions. Exposures of less than one year were not considered, and only exposures five to 45 years prior to diagnosis were considered pertinent for the cases. For the controls, the window of time during which exposures were considered had been determined based on the time of diagnosis of the patients in earlier studies.

None of the cases, and only four controls reported exposure to creosote. Assuming a null hypothesis for association of creosote with HD or NHL, the number of cases expected to report creosote exposure would be 2.4 based on the number of controls reporting creosote exposure and the ratio of cases to controls. This study shows no evidence of an association of creosote exposure with these diseases.

4.2.4.5 Tynes et al. (1994)

A nested case-control study was conducted to assess the presence of an association between exposure to electromagnetic fields existing at Norwegian railways and occurrence of brain tumors or leukemia in railway workers. Limited information on exposure to creosote was collected for analysis as a confounder.

The cohort from which the cases were selected included 13,030 male railroad workers employed in 1957 on either electric or non-electric railways and included line workers, outdoor station workers, and electrical workers. The cases identified from the Norway Cancer Registry to which all new cancer cases are reported included men diagnosed with brain tumors or leukemia during the follow-up period between 1958 and 1990. Four or five controls were selected for each case matched on year of birth. Controls were required to survive to the age at which the matching case was diagnosed. Information on whether the participants ever smoked was collected through telephone interviews.

Assessment of exposures to electromagnetic fields for the cases and controls was based on job titles, work histories, and job descriptions. Exposures to other potential hazards, including creosote, were estimated and analyzed as confounders. An exposure matrix was constructed using categories of exposure frequency (0=never, 1=monthly, 2=weekly, 3=daily) and years of employment as factors.

No association of brain tumors or leukemia with estimated exposure to creosote was observed in this study. As is true in many similar studies, assessment of exposures was based on qualitative information relevant to jobs and departments, and therefore is not precise, or accurate for any particular individual.

4.2.4.6 Schildt et al. (1999)

Associations between a number of occupational exposures including creosote with oral cancer was investigated in a case-control study in Sweden. The population-based study included 410 verified cases of squamous cell oral cancer reported to a four-county cancer registry during 1980-1989 and 410 controls drawn from a national population registry. Among the cases (175 alive, 235 deceased) were 134 women and 276 men. A control was matched to each case on age, gender, and county of residence. For deceased cases, deceased controls were selected from the the National Registry for Causes of Death. In addition to the other matching criteria, deceased controls also were matched on year of death.

Assessment of exposures was based on information collected through mailed questionnaires. For deceased participants, the questionnaire was sent to the next-of-kin in the order of spouse, child, parent, sibling, or other. The questionnaire included a lifetime work history and other questions concerning exposure factors of interest for oral cancer. Exposures associated with occupations held for less than one year were ignored.

Analysis of association between exposure to creosote and oral cancer showed no increased risk (OR = 0.5, CI = 0.1-2.0). The reliability of this result is weakened by the method of exposure assessment and by the small numbers of individuals exposed (three cases and six controls).

4.3 SUMMARY AND CONCLUSIONS OF THE HEALTH EFFECTS OF CREOSOTE IN HUMANS

Creosote and creosote-containing substances are widely used in industry and by certain subgroups of individuals, resulting in a large population of persons with potential exposure. According to California data, the majority of poisoning incident cases occurred as a result of handling creosote and applying it to wood without proper protection for the skin and eyes. The number of these cases has dropped quite markedly in the 1990s. Substantial contact with treated wood appears to be a risk factor for skin and eye burns, even years after the wood was treated. Symptoms experienced were burns and rashes on the exposed body areas, chemical conjunctivitis, headaches, nausea, and eye irritation.

While a number of human health studies are available that include creosote as a possible, or even likely, target exposure, few studies are available with enough information for a rigorous assessment of chronic health effects attributable to creosote specifically. By far, the most common limitation of studies aimed at evaluating effects of creosote exposure is the almost total absence of objective exposure measurements for the study participants. For most of the studies, assessment of exposure is based on information about past occupational activities provided by the participants or assigned by health studies professionals such as industrial hygienists with general knowledge of occupations and materials. In almost all cases, possible exposure to other materials, either separately or concomitantly, cannot be excluded. A second important limitation often seen in studies on effects of creosote is the lack of statistical significance calculated for many of the apparent associations between assigned creosote exposure and development of disease.

These limitations notwithstanding, among the epidemiological studies on effects of creosote exposure, increased risks for development of a number of diseases have been observed. Diseases typically found to be in excess include skin cancer and nonmalignant skin disorders, bladder cancer, lung cancer and nonmalignant respiratory diseases. Considering the information presently available, conclusions regarding chronic health effects from exposure to creosote alone should be considered tentative.

Table 4-4. Health studies in workers and non-workers exposed to creosote

Date	Journal	Author(s)	Study type	Population			Exposure Pure/ Mixed	Effects	
				Location	Category	N		Health	Other
1975	Journal of Occupational Medicine	Garrett	Case series	CA	Patient	2	Pure	Two patients with bladder cancer had histories of chronic exposure to cresol and creosote	
1979a	Koppers Company, Inc. Report	Tabershaw Occupational Medicine Associates	Cross-sectional	PA, SC,WV, KY	Occup	257	Mixed	Excess pustular eruptions of skin. Occasional borderline abnormalities. No evidence of cancer associated with employment.	
1979b 1979c 1980a 1980b 1980c	Koppers Company, Inc. Report	Tabershaw Occupational Medicine Associates	Cross-secional	CA, WV, AL, OH, IL	Occup		Mixed	Increased prevalence of folliculitis and tar warts consistent with prolonged exposure to coal tar products. Excess restrictive respiratory deficit. No excess cancer.	
1981	NIOSH HHE 80-238-931	NIOSH (work by Baker and Fannick)	Cross-sectional	NY	Occup	5	Pure	No chronic effects reported or observed. Acute skin problems reported or observed included irritation, desquamation, itching, cracking, and erythema. On hot days, burning, swollen or puffy eyes, and photophobia were reported.	
1981	EPA-OTS 86-870001567	Tabershaw Occupational Medicine Associates	Cross-sectonal	OH	Occup	59	Mixed	No evidence of disease associated with past exposure to creosote.	

Table 4-4. Health studies in workers and non-workers exposed to creosote

Date	Journal	Author(s)	Study type	Population			Exposure Pure/ Mixed	Effects	
				Location	Category	N		Health	Other
1986	EPA-OTS 86-870001566	Tabershaw Occupational Medicine Associates	Cross-sectional	SC	Occup	113	Mixed	No evidence of skin, bladder, or lung cancer. No evidence of kidney disease or blood disease. Liver disease observed in two workers. Greater than expected pustular eruptions.	
1981	EPA-OTS 86-870001549	Tabershaw Occupational Medicine Associates	Cohort mortality	IL, WV, CA, NJ, TX, AL, OH	Occup	4,048	Mixed	SMRs for all cancers and other cause-specific cancers increased.	
1982	EPA-OTS 86-870001547	Tabershaw Occupational Medicine Associates	Cohort mortality	IL, WV, CA, NJ, TX, Al, OH	Occup	3,254	Mixed	SMRs for all cancers and other cause-specific cancers increased.	
1989	American Journal of Industrial Medicine	Steineck et al.	Cohort	Sweden	Occup	1,905,660	Mixed	Increased relative risk for bladder cancer in population assigned exposure to creosote based on self-reported occupation in 1960.	
1992	Scandinavian Journal of Work and Environmental Health	Karlehagen et al.	Cohort incidence	Sweden and Norway	Occup	922	Pure	Increased risks for lip cancer, nonmelanoma skin cancer, malignant melanoma, and malignant lymphoma observed for men employed at creosote plants.	

Table 4-4. Health studies in workers and non-workers exposed to creosote

Date	Journal	Author(s)	Study type	Population			Exposure Pure/ Mixed	Effects	
				Location	Category	N		Health	Other
1987	American Journal of Industrial Medicine	Flodin et al.	Case-control	Sweden	Occup	131/431	Mixed	Analysis of risk factors for multiple myeloma showed crude ratios increased for occupational exposure to creosote, engine exhausts, and fresh wood.	
1989	British Journal of Industrial Medicine	Persson et al.	Case-control	Sweden	Public	160/275	Mixed	Crude and logistic ORs for HD and NHL increased for exposure to creosote (for HD, ORs 10.5 and 10.7, for NHL, OR 13.6 and 9.4)	
1992	Cancer Causes and Control	Feingold et al.	Case-control	CO	Public	252/222	Mixed	Odds ratios for association of total childhood cancer and childhood brain cancer with exposure of father to creosote during year prior to child's birth = 2.5 (ns) and 3.7 (ns).	
1993	Cancer	Persson et al.	Case-control	Sweden	Public	124/204	Mixed	None	None of 124 patients and four of 204 controls reported exposure to creosote
1994	American Journal of Epidemiology	Tynes et al.	Nested case-control	Norway	Occup	92/442 (Cohort 13,030)	Mixed	No association between brain tumors or leukemia and exposure to creosote observed.	
1999	Oncology Reports	Schildt et al.	Case-control	Sweden	Public	410/410	Mixed	No association between oral cancer and exposure to creosote observed	

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